

Specific sensitization in wheat flour and contributing factors in traditional bakers

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Abstract. – Skin prick tests (SPTs) play an important role in the diagnosis of bakers asthma and epidemiological field studies on frequencies of sensitization to wheat or rye flour.

In many epidemiological studies the investigators have tried to reveal the determinants of specific sensitization, and atopy appears to be a very strong determinant for sensitization to flour allergens. Age and gender have not reported to be determinants of sensitization. Only one study found that sensitization in wheat flour with skin prick test was significantly associated with cigarette smoking.

Few data are available on sensitization to wheat flour in populations without occupational exposure to bakery allergens.

The aim of this study was to investigate the sensitization of wheat flour and other baking allergens (oat, barley, and rye flour) in traditional bakers and in cleaners in a big hospital in the same area. In addition the correlation of atopy with specific sensitization and the correlation of specific sensitization with age, sex, working hours, working years, smoking status and pack/years with use of skin prick tests.

Key Words:

Skin prick test, Bakers, Sensitization, Flour.

In many epidemiological studies the investigators have tried to reveal the determinants of specific sensitization, and atopy appears to be a very strong determinant for sensitization to flour allergens. The reported OR (odds ratio) for atopy range for 4.4 to 20.8². Age and gender have not reported to be determinants of sensitization. Only one study found that sensitization in wheat flour with skin prick test was significantly associated with cigarette smoking (OR: 2.7)³.

Few data are available on sensitization to wheat flour in populations without occupational exposure to bakery allergens. Houba et al⁴ reported skin prick tests with wheat flour in 416 laboratory animal workers and found a positive test in 2.1%. Gautrin et al⁵ found that 1.2% and 4.1% of apprentices in animal health and dental hygiene, respectively were sensitized to wheat flour, and Droste et al found that the wheat sensitization in employees in petrochemical plant was 0.4%⁶.

The aim of this study was to investigate the sensitization of wheat flour and other baking allergens (oat, barley, and rye flour) in workers in bakeries in Patras and in cleaners in a big hospital in the same area, the correlation of atopy with specific sensitization and the correlation of specific sensitization with age, sex, working hours, working years, smoking status and pack/years with use of skin prick tests.

Introduction

Skin prick tests (SPTs) play an important role in the diagnosis of bakers asthma and epidemiological field studies on frequencies of sensitization to wheat or rye flour.

Sensitization frequencies to wheat flour by SPTs in epidemiological studies of bakers varied 4 to 20% (Table I). This may be caused at least partially by different test extracts containing a varying amount of the relevant single allergen¹.

Material and Methods

Study Design

The current study was designed as a cross-sectional study among 58 workers from small traditional bakeries in city of Patras, in south west of Greece, who involved in production of bread in dusty work place, and 45 workers from the same bakeries who involved exclusively with

Table I. Sensitization in bakery allergens in bakers in cross sectional studies with use of skin prick tests.

Study	Sensitization in wheat flour	Sensitization in rye flour	Sensitization in barley flour	Sensitization in oat flour	Sensitization in any bakers allergen
Prichard et al 1984 ¹¹	15%	–	–	–	–
Musk et al 1989 ⁹	5%	–	–	–	9%
Bohadana et al 1994 ¹⁸	11%	–	–	–	–
Cullinan et al 1994 ¹⁹	5%	–	–	–	–
De Zotti et al 1994 ⁴³	12%	–	–	–	21.7%
Zuskin et al 1994b ²⁰	12%	–	–	–	–
Houba et al 1996b ⁴	8%	–	–	–	–
Smith et al 1997 ²¹	6%	–	–	–	–
Pavlovic et al 2001 ²²	12%	–	–	–	15%
Cullinan et al 2001 ¹⁵	7%	–	–	–	15%
Talini et al 2002 ¹²	20%	–	–	–	–
Droste et al 2003 ⁶	12.4%	3.3%	–	–	15.4%
Storaas et al 2005 ¹³	4%	1.0%	3%	1.0%	15%

sells of bread, in work places without dust flour and in different working hours. They are white Caucasians with the same socioeconomic status.

The reference population who we were used for comparison in regard to prevalence of specific sensitization with the other two groups who mentioned above, was workers (n = 45) from cleaning company in a big hospital in the same area and they had never contact with flour. The study was approved by the Patras Hospital Research Ethics Board and written informed consent was obtained for each patient. Data collection was conducted between July 2003 and May 2006.

Questionnaire

Data on respiratory and allergy related symptoms were collected by means of validated respiratory questionnaire⁷, administered by an occupational physician, supplement with questions of acute work related respiratory symptoms, demographic and occupational characteristics. Questions on smoking history were based upon ERCS questionnaire⁸.

Smoking status was categorized as never smoker and current smoker. Current smokers were defined as those who smoked at least one cigarette daily or one cigar weekly for a period of 1 year and who were still smoking within 1 month before the examination. All other subjects were considered as never smokers. Ex-smokers were excluded from the study. We also calculate the index of pack/years with multiply the number of pack cigarettes with years smoking.

Skin Prick tests

Skin prick tests were performed by dermatologist by standard procedures in a particular room of hospital of Patras. Tests performed on the flexor surface of the forearm using following common allergen extracts (Test Kit – Allergopharma, Doctum, Greece), such house dust mites (*Dermatophagoides Farinae*, *Dermatophagoides Pteronyssinus*), animal dander (cat, dog), molds (*Alternaria tenuis*, *Aspergillus fumigatus*, *Cladosporium herbarum*), pollen (grass, grasses/cereals, birch), and the following baking allergens (wheat flour, rye flour, barley flour, and oats flour). We also use a histamine phosphate at 10mg/ml and normal saline as positive and negative controls respectively.

Wheal diameters were recorded 20 minutes after application of the antigens. Mean diameters were calculated as the mean of the widest diameter and the perpendicular diameter measured at its midpoint. Based upon the distribution of the responses to the positive control, a mean wheal response diameter of at least 3mm was considered as a positive response.

Atopy defined as having one or more positive skin test response in common allergens (house dust mites, cat, dog and pollen). Specific sensitization defined as having one or more positive skin response in bakery allergens (wheat, rye, oat or barley).

Workers with pathological changes of skin around the test area, pregnancy, and simultaneous therapy with beta-blockers or ACE inhibitors were excluded of the study. Although

SPTs are safe tests, the following emergency resuscitative equipment was available (injectable adrenaline 1:1000, oxygen, oral phenergan and injectable phenergan, hydrocortisone and inhaled bronchodilator). All antihistamine containing medications stopped 24 prior the testing. The persons were outpatient and the tests began at 09.00 h.

Statistics

Statistical analysis was carried out with a statistical software package “SPSS” version 10.0 and included calculation of the proportion and the percentages, distribution control for scale variables, calculation and comparison of means (t-test with confidence interval 95% for variables with normal distribution and Mann-Whitney u-test for variables without normal distribution). Application of Pearson’s correlation method (chi-square analysis) was the statistical tool of our study in order to evaluate the relationships between nominal variables.

Results

The anthropometric characteristics of three groups that were studied are shown on Table II. Based on the results, the bakers were statistically older from the bread salesclerks ($p = 0.02$), but

not from the cleaners ($p = 0.073$). They were statistically taller than the other two groups ($p = 0.013$, $p < 0.01$, respectively.) and also statistically heavier ($p = 0.038$, $p < 0.01$).The percentage of men who worked in the baker’s group was statistically larger in comparison to the other two groups ($p < 0.01$), and they worked statistically more years than the sale clerks and the cleaners ($p < 0.01$). They also smoke more pack years in comparison to both other groups ($p < 0.01$).

The percentage of atopy and the specific sensitization of the three under observation groups are shown on Table III. It was found that all three groups were not different on atopy (sensitization at least one common allergen). Bakers were more sensitive on bakery allergens on which they were examined (at total), in comparison to the bread salesclerks and cleaners ($p = 0.01$) and in greater percentage sensitive on wheat flour (17.24%), rye flour (10.34%), barley flour (8.62%) and oat flour (13.79%) in comparison with the two others groups. There was no difference on the percentage of sensitization for the total of allergens of bakery and for each one separately among the salesclerks and cleaners.

An attempt to find a correlation among the specific sensitization with atopy, sex, age, weight, height, working hours, working years, smoking status and pack/years for the group of bread producers and salesclerks was shown on Tables 4 and 5.

Table II. Sensitization in bakery allergens in bakers in cross sectional studies with use of skin prick tests.

Characteristics	Bread producers (A)	Salesclerks (B)	Cleaners (C)	P value (A-B)	P value (A-C)	P value (B-C)
Number of subjects	58	45	45			
Mean age in years (SD)	43 (12.50)	37.91(9.48)	38.89(9.89)	*	≥ 0.05	≥ 0.05
Height (cm) (SD)	172.66 (8.0)	168.38 (9.05)	165.96 (5.7)	*	**	≥ 0.05
Weight (kg)(SD)	78.76 (15.71)	72.42 (14.36)	64.89 (12.89)	*	**	*
Mean numbers of years employed (SD)	20.57 (11.55)	11.38 (7.95)	3.42 (3.57)	**	**	**
Mean number of hours per day employed (SD)	9.86 (2.44)	9.0 (2.1)	8.22 (1.11)	*	**	*
Smoking status						
Current smoker (%)	49 (84.49)	34 (75.6)	37 (82.2)	≥ 0.05	≥ 0.05	≥ 0.05
Never smoker (%)	9 (15.51)	11 (24.4)	8 (17.8)	≥ 0.05	≥ 0.05	≥ 0.05
Pack/years (SD)	25.29 (28.25)	8.47 (8.56)	10.71(12.01)	**	**	≥ 0.05
Gender						
Male (%)	82.75%	31.1%	6.6%	**	**	**
Female (%)	17.25%	68.9%	93.4%	**	**	**

* $P < 0.05$; ** $P < 0.01$; P values is for different comparison of means.

Table III. Prevalence of atopy and specific sensitization in bakery allergens in the three groups with use of skin prick tests.

Characteristics	Bread producers (A)	Salesclerks (B)	Cleaners (C)	P value (A-B)	P value (A-C)	P value (B-C)
Number of subjects	58	45	45			
Atopy (%)	39.7	37.8	40.0	0.848	0.972	0.831
Sensitization at least to one bakery allergen	22.41	4.4	4.4	*	*	0.404
Sensitization in wheat flour	17.24	2.2	2.2	*	*	0.562
Sensitization in rye flour	10.34	0.0	2.2	*	*	0.156
Sensitization in barley flour	8.62	0.0	2.2	*	*	0.312
Sensitization in oat flour	13.79	2.2	0.0	*	*	0.156

* $P < 0.05$.

Based on the findings of the foresaid tables there was a correlation between the atopy and the sensitization to the allergens of bread (OR: 15.12, 95% CI = 2.54-116.65) in total, as well as, correlation between the atopy and the sensitization in wheat flour (OR: 8.8, 95% CI = 1.44-68.94) for bakers.

In contrast, for the group of the bread salesclerks there was found no correlation for the specific sensitization to all allergens of bakery ($p = 0.066$) and also for sensitization to wheat flour ($p = 0.203$). It was also found that there was a correlation between the smoking status of the bread makers and the sensitization in wheat flour ($p = 0.018$), as well as correlation between the smoking status and the sensitization of the salesclerks

to the allergens of bakeries in total ($p = 0.01$). No correlation between sex, age, working hours, working years and pack/years and specific sensitization in two groups was found.

On Tables 6 and 7 can be an attempt to find a correlation between the specific sensitization to bakery allergens with working years ≥ 10 and pack/years in the bread makers and salesclerks.

Therefore it can be seen that in regard to working years (more than 10 years) of the bread makers there was a correlation to the sensitization to rye flour ($p = 0.041$) and to oat flour ($p = 0.015$) but no such correlation to the group of bread salesclerks. Also there were no correlation between pack/years ≥ 20 and specific sensitization in two groups.

Table IV. Correlation between specific sensitization in bakery allergens with atopy, sex, age, working hours, working years, smoking status, and pack/years in bakers (n = 58).

	Sensitization in one at least bakery allergens P value	Sensitization in wheat flour P value	Sensitization in rye flour P value	Sensitization in barley flour P value	Sensitization in oat flour P value
Atopy	.000**	.004**	.001**	.003**	.000**
Sex	.535	.804	.245	.294	.540
Age	.425	.127	.258	.394	.349
Working hours	.088	.072	.885	.610	.449
Working years	.444	.121	.133	.263	.110
Smoking status	.087	.018*	.210	.118	.434
Pack/years	.228	.074	.579	.726	.192

*Correlation is significant at the 0.05 level; ** Correlation is significant at the 0.01 level.

Table V. Correlation between specific sensitization in bakery allergens with atopy, sex, age, working hours, working years smoking status and pack/years in salesclerks (n = 45).

	Sensitization in one at least bakery allergens <i>P</i> value	Sensitization in wheat flour <i>P</i> value	Sensitization in rye flour <i>P</i> value	Sensitization in barley flour <i>P</i> value	Sensitization in oat flour <i>P</i> value
Atopy	.066	.203	-a	-a	.203
Sex	.342	.508	-a	-a	.508
Age	.471	.178	-a	-a	-a
Working hours	.497	.636	-a	-a	-a
Working years	.168	.292	-a	-a	-a
Smoking status	.067	.078	-a	-a	.078
Pack/years	.154	.323	-a	-a	-a

*Correlation is significant at the 0.05 level; **Correlation is significant at the 0.01 level; -a cannot be computed because at least one of the variables is constant.

Discussion

The larger portion of bakery shops in Greece in a traditional way, both in the division of labor and in the technological standards. Specifically, the number of employees in a bakery in our country is between 2 to 5 people and a self-employed owner. Usually technology in traditional bakers is not as developed as in industrial bakeries and often a lot of work is manual. For the production of bread in Greek bakeries, workers used flour which derived in greater percentage from wheat, and in minor percentage from rye, barley and oat.

At the total number of the employees in the preparation of bread, 1 to 2 persons work for the bread making that takes place very early in the morning (usually 03.00 to 08.00) and the others are working only on selling the bread. Selling the bread takes place on different hours (usually 08.00-14.00) and in place inside the bakery but away from the place of the production, in order

to minimize the inhalation of dust flour, which is responsible, according to the international bibliography⁹, for the immunological sensitization of the employees to the bakery allergens (e.g. wheat flour, rye flour) and this results to respiratory sensitization (cough, rhinitis, conjunctivitis due to occupation and occupational asthma) of the employees.

According to the international studies, responsible for the immunological sensitization of the bread makers to the bakery allergens are important factors such as atopy and the strength exposure to the dust flour. Also there is one study that was found correlation between the specific sensitization and smoking habit³.

In this study we were looking up for the percentage of sensitization of the employees in the production of bread in traditional bakeries in Greece, using SPTs on a group of salesclerks and a group of cleaners who have no contact with dust flour. We used for the determination of specific sensitization the skin prick tests instead

Table VI. Correlations between specific sensitization to bakery allergens with working years ≥ 10 and pack/year's ≥ 20 in bread producers (n = 58).

	Sensitization in one at least bakery allergens <i>P</i> value	Sensitization in wheat flour <i>P</i> value	Sensitization in rye flour <i>P</i> value	Sensitization in barley flour <i>P</i> value	Sensitization in oat flour <i>P</i> value
Working years ≥ 10	.225	.928	.041*	.216	.015*
Pack/years ≥ 20	.202	.066	.125	.220	.588

*Correlation is significant at the 0.05 level; **Correlation is significant at the 0.01 level.

Table VII. Correlation between specific sensitization in bakery allergens with working years ≥ 10 and pack/years ≥ 20 in salesclerks (n = 45).

	Sensitization in one at least bakery allergens <i>P</i> value	Sensitization in wheat flour <i>P</i> value	Sensitization in rye flour <i>P</i> value	Sensitization in barley flour <i>P</i> value	Sensitization in oat flour <i>P</i> value
Working years ≥ 10	.875	.268	-a	-a	.377
Pack/years ≥ 20	.660	.759	-a	-a	.759

*Correlation is significant at the 0.05 level; **Correlation is significant at the 0.01 level; a- cannot be computed because at least one of the variables is constant.

serological IgE, because based in study of Maja-maa et al¹⁰, suggested that sensitivity and specificity are greater for SPTs than RAST tests (0.23 v 0.20 and 1.0 v 0.93 respectively).

The atopy in bakers in our study was 39.7%, result which agree with the other studies^{9,11,12}.

It was therefore seen that the employees in the bread production are sensitive to wheat flour in a percentage 17, 24% which agrees with the percentage found on the international studies for the bread producers (Table I, percentage 4 to 20%). This range among the different studies is based upon the methods used which varied from study to study, the extracts that are available for bakery allergens are not standardized, and the origin and concentration of the extracts used for skin prick testing are quite different. In spite of these differences in research methodology, the available studies clearly show that the immunologic sensitization in wheat flour with skin prick testing is common among bakery workers¹¹. In our study it was found 17.24%, significant greater ($p = 0,014$, OR: 9.16, 95% CI = 1.12-199.14) versus 2.2% for the salesclerks.

Also the specific sensitization in rye flour, oat flour and barley flour in bread producers was significant greater, comparison with specific sensitization in those bakery allergens in the salesclerks. The only study which investigated the specific sensitization in oat flour, rye flour and barley flour in bakers performed from Storaas et al¹³, and the results was that the specific sensitization in wheat flour was more frequent.

Very few studies used as control group individuals that have no relation with bakery allergens. In these studies the percentage of specific sensitization of control groups vary among 0.4-4.1%^{3,5,6}. These studies suggest that there is at least some background level of sensitization in the general population, probably due an increased propensity to develop IgE mediated

sensitization in individuals with immunologic sensitization to common allergens (atopy), or as a result from cross-reactivity to other allergens⁶. In our study, the percentage of cleaners with specific sensitization in bakery allergens was 2.2% also.

In the group of bread makers it was found a correlation among the atopy and specific sensitization to all allergens of bakers ($p < 0.01$, OR = 15.12) and wheat flour ($p < 0.01$, OR = 8.8). The result found matches with the review of Houba et al², where the odds ratio for atopy varies among 5.1 to 20.8. No such correlation was found for the group of salesclerks. That result corresponded to the opinion that the atopy is the most important determinant in specific sensitization in wheat flour.

It was also found that the smokers in the group of bread producers showed a slightly decreased risk of sensitization in wheat flour (OR: 0.17, 95% CI, 0,03-1.06), results which agree with study of Nieuwenhuijsen et al¹⁴, where the risk of sensitization was PR = 0.7, but no significant. Our result is different from the study of De Zotti et al³, where the authors found that the sensitization in bakery allergens in total was significantly associated with cigarette smoking with odds ratio 2.67. The different may be result that in the study of De Zotti investigated the correlation between specific sensitization in bakery allergens in total, whereas in our study investigate the specific sensitization in wheat flour. Also in our study we were excluded the ex smokers from the investigation and so the no smokers was only 9 persons, whichever the 4 was sensitive in wheat flour. Cullinan et al¹⁵ investigate that there was no evidence of a positive, independent effect of smoking on the development of a positive skin test.

Finally, an examination was carried out for the correlation between pack years and the spe-

cific sensitization. The only study that was found out in the international bibliography on the same topic was the study of Heederik et al¹⁶ who suggested that wheat sensitization was positively associated with current smoking (PR: 1.7) and with number of cigarette (2.8). In our study, an indicator of 20 pack/years was used because the bread bakers have an average of 25.2 pack/years, and we didn't find any correlation. However in that study (Heederik) the authors used for the definition of specific sensitization the determination the IgE-antibodies in the sera of bakers. The point is that the part played by smoking in the cutaneous response to allergens and in occupational asthma is not clear¹³.

In order to find the correlation among working years to the bakery and the specific sensitization to the bakery allergens, we used the employment above 10 years as indicator. We were based in study of Musk et al⁹, where it was found that there was a correlation among positive skin test to one or more bakery antigens (e.g. baker's yeast, mixed flour) and additional 10 years working in bakery with odds ratio 1.8. In our study was found that bread makers who worked more than 10 years had significant decreased risk for specific sensitization in bakery allergens (OR: 0.16, 95% CI for oat flour, and OR: 0.18, 95% CI, for rye flour, respectively). That result may be due to abandonment of workplace from workers because of their pronounced symptomatology which developed usually after the first years of working as a baker.

The conclusion was that the bread producers were more sensitive to wheat flour than the group of salesclerks (OR: 9.1, 95% CI 1.12-199.14) due to atopy (OR: 8.8, 95% CI 1.44-68.94). It is therefore reasonable that individuals who are atopic should not work as bread makers because there is a greater risk for sensitization to allergens of bakeries and respiratory work related symptoms. Nevertheless, atopic persons should be informed about their increased risk of developing occupational respiratory disease and the best moment for that is before they start the vocational training. Also education in environmental prevention is particularly important in small business, where the baking procedures are less automated and clearly periodical medical checks should be performed, and the removal of symptomatic workers from the offending atmosphere is the treatment of choice.

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